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## **J-shaped association between plasma glucose concentration and cardiovascular disease mortality over a follow-up of 32 years**

von Gunten, Elisabeth ; Braun, Julia ; Bopp, Matthias ; Keller, Ulrich ; Faeh, David

**Abstract:** **OBJECTIVE:** We aimed at examining the association between plasma glucose (PG) concentration and cardiovascular mortality in a population sample from Switzerland over a follow-up time of 32 years. **METHODS:** We analyzed 7984 men and women enrolled in the first National Research Program (NRP1A, 1977-1979) and followed up for survival until 2008. Mortality hazard ratios (HR) were calculated using adjusted Cox regression models. PG was measured in fasting state or randomly with known fasting time. Models were adjusted for age, sex, socio-demographic, lifestyle and cardiovascular risk factors. **RESULTS:** PG concentrations  $\geq 6.1$  mmol/L were associated with increased risk of cardiovascular disease (CVD) and all-cause mortality. Compared to normal PG (3.8-4.9 mmol/L) the adjusted HR (95% CI) for CVD mortality was 1.26 (1.01-1.58) for PG 6.1-6.9 mmol/L, 1.56 (1.18-2.06) for PG  $\geq 7$  mmol/L, 1.67 (1.22-2.30) for known diabetes. All-cause mortality essentially showed the same patterns. All-cause mortality was increased [HR (95% CI): 1.35 (1.01-1.80)] also for PG  $< 3.8$  mmol/L. **CONCLUSION:** Plasma glucose remained significantly and independently associated with CVD mortality even after full follow-up. The relationship was J-shaped. In order to prevent premature death, persons with abnormal PG concentrations on both extremes should be screened and counseled for other CVD risk factors.

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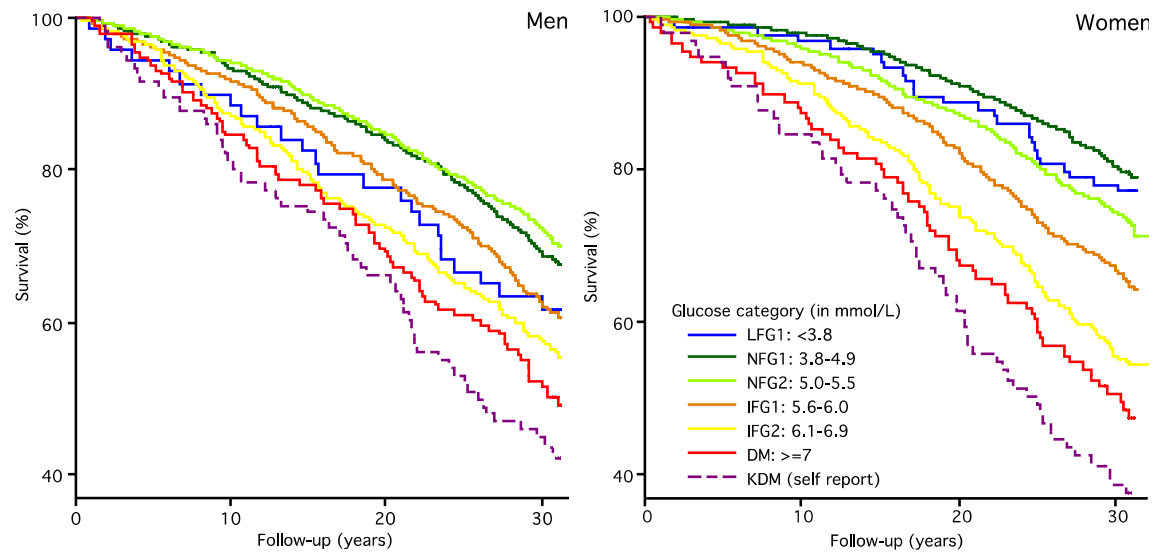
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## SUPPLEMENTARY MATERIAL FOR

### Association of a single measurement of plasma glucose concentration and cardiovascular disease mortality over a follow-up of 32 years

**Figure S1.** Kaplan-Meier survival curves for all-cause mortality, by glucose category and sex, 7,984 participants of NRP 1A in Switzerland 1977-1979, 16-92 years at baseline



**Table S2.** Characteristics of the study population, by glucose category and sex

	<b>LFG</b>	<b>NFG1</b>	<b>NFG2</b>	<b>IFG1</b>	<b>IFG2</b>	<b>DM</b>	<b>KDM</b>
	<b>&lt;3.8</b>	<b>3.5-4.9</b>	<b>5.0-5.5</b>	<b>5.6-6.0</b>	<b>6.1-6.9</b>	<b>≥7</b>	
<b>Men</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	
Participants (n)	69	973	1229	685	378	171	102
Participants (in % of total, by sex)	1.9	27.0	34.1	19.0	10.5	4.8	2.8
Dropped due to missing values*	1	22	15	17	12	5	4
Age (mean, years)	40.5	40.4	40.3	44.1	45.0	47.6	48.6
Follow-up (mean, years)	23.6	25.8	25.9	24.5	23.8	22.2	21.8
Mortality							
All-cause deaths (n)	25	292	340	252	157	81	54
All-cause deaths (% of total, by sex)	36.2	30.0	27.7	36.8	41.5	47.5	52.9
Person-years (py)	1629	25077	31879	16776	9010	3802	2223
Age standardized rate (per 100,000 py)	839	1191	792	820	1035	1423	1210
CVD deaths (n)	5	109	128	99	57	31	20
Cancer deaths (n)	8	85	121	74	39	23	17
Fasting time (h, mean)	3.5	4.4	4.7	4.7	3.6	3.2	4.3
Fasting <2h (% of total n, by sex)	43.5	22.5	18.3	24.7	41.3	50.3	25.5
Lifestyle							
Three main meals per day (%)	66.7	66.1	65.7	67.7	61.6	66.7	63.7
Physical activity score (0-8, mean)	3.8	3.9	3.9	3.7	3.7	3.6	2.9
Smoking							
Current smokers (≥1 cig/d, %)	50.7	39.3	34.2	34.7	37.3	37.4	31.4
Number of cigarettes (mean, among smokers)	14.0	16.6	18.3	19.4	20.1	17.5	15.3
Blood pressure							
Mean systolic (mmHg)	126	128	129	132	134	134	136
≥140/≥90 mmHg (systolic/diastolic, %)	24.6	23.0	24.3	31.4	38.1	35.7	37.3
Total cholesterol							
Mean (mmol/l)	5.7	5.8	6.0	6.0	6.0	6.0	6.0
>6.2mmol/l (%)	13.0	21.5	28.1	27.6	31.0	29.8	37.3
Body mass index							
Mean (kg/m <sup>2</sup> )	23.7	24.5	24.8	25.0	25.1	25.6	25.7
Overweight (≥25, %)	4.4	5.6	6.5	7.6	8.2	12.3	14.7
Marital status							
Single (%)	29.0	24.2	22.1	19.3	16.1	14.6	17.7
Married (%)	70.0	72.3	73.7	75.0	77.3	74.9	75.5
Widowed (%)	0.0	1.3	1.0	1.3	2.4	2.9	2.0
Divorced or separated (%)	1.5	2.3	3.3	4.4	4.2	7.6	4.9

	<b>LFG</b>	<b>NFG1</b>	<b>NFG2</b>	<b>IFG1</b>	<b>IFG2</b>	<b>DM</b>	<b>KDM</b>
	<b>&lt;3.8</b>	<b>3.5-4.9</b>	<b>5.0-5.5</b>	<b>5.6-6.0</b>	<b>6.1-6.9</b>	<b>≥7</b>	
<b>Women</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	<b>mmol/l</b>	
Participants (n)	120	1502	1321	673	350	131	96
Participants (in % of total, by sex)	2.9	35.8	31.5	16.1	8.4	3.1	2.3
Dropped due to missing values*	3	34	40	16	10	4	1
Age (mean, years)	38.5	39.4	43.5	46.7	49.4	53.0	52.4
Follow-up (mean, years)	26.4	27.8	26.8	25.6	24.3	22.8	21.2
Mortality							
All-cause deaths (n)	26	291	342	222	150	65	56
All-cause deaths (% of total, by sex)	21.7	19.4	25.9	33.0	42.9	49.6	58.3
Person-years (py)	3152	41809	35419	17296	8513	3018	2051
Age standardized rate (per 100,000 py)	409	691	446	511	691	596	830
CVD deaths (n)	5	109	128	99	57	31	20
Cancer deaths (n)	10	96	112	55	39	17	19
Fasting time (h, mean)	3.5	4.2	4.4	4.1	3.5	2.9	4.6
Fasting <2h (% of total n, by sex)	40.0	22.9	20.0	22.0	28.3	41.2	15.6
Lifestyle							
Three main meals per day (%)	77.5	71.8	75.1	73.3	74.0	72.5	77.1
Physical activity score (0-8, mean)	3.9	3.5	3.4	3.3	3.0	2.9	2.8
Smoking							
Current smokers (≥1 cig/d, %)	27.5	28.2	24.6	24.4	26.0	21.4	16.7
Number of cigarettes (mean, among smokers)	12.4	12.4	12.4	11.9	14.7	14.4	14.6
Blood pressure							
Mean systolic (mmHg)	117	121	125	128	132	134	132
≥140/≥90 mmHg (systolic/diastolic, %)	10.8	14.3	21.8	24.5	32.3	35.9	34.4
Total cholesterol							
Mean (mmol/l)	5.7	5.8	6.0	6.1	6.1	6.1	6.1
>6.2mmol/l (%)	14.2	22.4	28.8	33.7	36.9	38.2	39.6
Body mass index							
Mean (kg/m2)	22.3	22.7	23.5	23.7	24.3	25.0	25.5
Overweight (≥25, %)	2.5	3.8	6.4	6.7	11.7	15.3	14.6
Marital status							
Single (%)	24.2	24.5	19.0	20.2	19.1	22.1	19.8
Married (%)	74.2	65.9	68.3	64.2	61.1	58.8	60.4
Widowed (%)	0.8	5.0	7.7	10.3	14.3	13.0	16.7
Divorced or separated (%)	0.8	4.6	5.1	5.4	5.4	6.1	3.1

Population sample: 7,984 participants, 3,683 male and 4,301 female of NRP 1A, Switzerland 1977-1979, 16-92 years at baseline,

\* 184 persons dropped due to missing values in the variables fasting time, marital status, three main meals per day, physical activity score, BMI and blood pressure

Glucose categories: LFG: <3.8 mmol/L, NFG1: 3.5-4.9 mmol/L, NFG2: 5.0-5.5 mmol/L, IFG1: 5.6-6.0 mmol/L, IFG2: 6.1-6.9 mmol/L, DM: Diabetes  $\geq 7$  mmol/L, KDM: Known diabetes. Reference: NFG1: 3.8-4.9 mmol/L

**Table S3.** Trends (p-value and z-value) between increasing plasma glucose category and covariates

<b>Men</b>	<b>Trend p*</b>	<b>Trend z*</b>
Age (years)	<i>0.000</i>	8.16
Fasting time (h)	<i>0.000</i>	-4.99
Three main meals per day (%)	<i>0.620</i>	-0.50
Physical activity score (0-8)	<i>0.001</i>	-3.44
Systolic blood pressure (mmHg)	<i>0.000</i>	8.77
Cholesterol (mmol/l)	<i>0.000</i>	7.17
Body mass index (kg/m2)	<i>0.000</i>	5.38
Smoking (cig/day)	<i>0.177</i>	-1.35
Marital status*	<i>0.002</i>	40.70
<b>Women</b>	<b>Trend p</b>	<b>Trend z</b>
Age (years)	<i>0.000</i>	15.43
Fasting time (h)	<i>0.010</i>	-2.57
Three main meals per day (%)	<i>0.191</i>	1.31
Physical activity score (0-8)	<i>0.000</i>	-6.75
Systolic blood pressure (mmHg)	<i>0.000</i>	13.98
Cholesterol (mmol/l)	<i>0.000</i>	11.65
Body mass index (kg/m2)	<i>0.000</i>	10.79
Smoking (cig/day)	<i>0.006</i>	-2.76
Marital status*	<i>0.000</i>	90.01

Population sample: 7,984 participants, 3,683 male and 4,301 female  
of NRP 1A, Switzerland 1977-1979, 16-92 years at baseline

\*Trends (p and z-value) for continuous variables were calculated  
using Stata's nptrend command, for the categorical variable marital  
status chi-square tests were used.

**Table S4.** Adjusted hazard ratios for all-cause, CVD, cancer and non-cancer-non-CVD mortality by glucose category and sex

	LFG <3.8		NFG1 3.8-4.9	NFG2 5.0-5.5		IFG1 5.6-6.0		IFG2 6.1-6.9		Diabetes ≥7.0 mmol/L		Known diabetes	
All	HR	(95% CI)		HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
All-cause mortality													
Model 1	1.38	(1.04-1.84)	1	1.06	(0.95-1.18)	1.06	(0.94-1.20)	1.31	(1.14-1.50)	1.39	(1.16-1.67)	1.65	(1.35-2.03)
Model 2	1.42	(1.06-1.89)	1	1.06	(0.94-1.18)	1.03	(0.91-1.17)	1.28	(1.11-1.47)	1.33	(1.11-1.60)	1.58	(1.29-1.95)
Model 3	1.35	(1.01-1.80)	1	1.04	(0.93-1.16)	1.01	(0.89-1.14)	1.19	(1.04-1.37)	1.27	(1.05-1.52)	1.55	(1.26-1.90)
CVD mortality													
Model 1	1.24	(0.77-1.98)	1	1.02	(0.85-1.23)	1.09	(0.89-1.32)	1.26	(1.01-1.58)	1.56	(1.18-2.06)	1.67	(1.22-2.30)
Model 2	1.29	(0.80-2.07)	1	1.03	(0.86-1.24)	1.06	(0.87-1.29)	1.23	(0.98-1.54)	1.47	(1.11-1.94)	1.63	(1.18-2.25)
Model 3	1.23	(0.77-1.99)	1	1.00	(0.83-1.20)	1.01	(0.83-1.23)	1.09	(0.87-1.37)	1.36	(1.03-1.80)	1.54	(1.11-2.12)
Cancer mortality													
Model 1	1.56	(0.96-2.53)	1	1.16	(0.95-1.41)	0.98	(0.78-1.24)	1.12	(0.86-1.47)	1.29	(0.91-1.82)	1.88	(1.31-2.70)
Model 2	1.55	(0.95-2.52)	1	1.16	(0.96-1.41)	0.98	(0.78-1.24)	1.11	(0.85-1.45)	1.26	(0.89-1.78)	1.85	(1.29-2.66)
Model 3	1.45	(0.89-2.37)	1	1.16	(0.95-1.41)	0.97	(0.77-1.22)	1.06	(0.81-1.38)	1.21	(0.85-1.71)	1.85	(1.29-2.67)
Non-cancer-non-CVD mortality													
Model 1	1.24	(0.72-2.13)	1	1.02	(0.84-1.24)	1.11	(0.90-1.39)	1.56	(1.22-1.98)	1.32	(0.94-1.87)	1.45	(0.97-2.18)
Model 2	1.29	(0.75-2.23)	1	1.01	(0.83-1.23)	1.06	(0.85-1.32)	1.52	(1.19-1.93)	1.27	(0.90-1.80)	1.35	(0.90-2.03)
Model 3	1.23	(0.71-2.13)	1	1.00	(0.82-1.22)	1.05	(0.84-1.31)	1.46	(1.15-1.86)	1.24	(0.87-1.75)	1.35	(0.89-2.03)
Men													
All-cause mortality													
Model 1	1.38	(0.91-2.07)	1	1.00	(0.85-1.17)	0.96	(0.81-1.14)	1.14	(0.94-1.39)	1.27	(0.99-1.62)	1.35	(1.01-1.81)
Model 2	1.40	(0.93-2.11)	1	1.00	(0.86-1.18)	0.94	(0.79-1.12)	1.14	(0.94-1.39)	1.20	(0.93-1.54)	1.28	(0.96-1.72)
Model 3	1.32	(0.87-1.99)	1	0.97	(0.83-1.13)	0.90	(0.76-1.07)	1.04	(0.85-1.27)	1.13	(0.88-1.45)	1.24	(0.92-1.67)
CVD mortality													
Model 1	1.65	(0.94-2.92)	1	0.95	(0.72-1.23)	0.90	(0.69-1.19)	1.17	(0.86-1.60)	1.41	(0.96-2.07)	1.59	(1.03-2.43)
Model 2	1.72	(0.97-3.03)	1	0.96	(0.74-1.26)	0.89	(0.67-1.17)	1.18	(0.86-1.61)	1.31	(0.88-1.94)	1.52	(0.99-2.34)
Model 3	1.69	(0.95-3.01)	1	0.90	(0.69-1.18)	0.82	(0.62-1.09)	1.02	(0.74-1.39)	1.16	(0.78-1.71)	1.38	(0.89-2.12)
Cancer mortality													
Model 1	1.59	(0.77-3.29)	1	1.18	(0.89-1.55)	0.99	(0.72-1.35)	0.97	(0.66-1.42)	1.22	(0.76-1.94)	1.52	(0.90-2.58)
Model 2	1.59	(0.77-3.30)	1	1.18	(0.89-1.56)	0.98	(0.71-1.34)	0.96	(0.65-1.40)	1.15	(0.72-1.84)	1.46	(0.86-2.47)
Model 3	1.46	(0.70-3.03)	1	1.15	(0.87-1.52)	0.94	(0.69-1.29)	0.89	(0.60-1.30)	1.09	(0.68-1.75)	1.48	(0.87-2.52)

Non-cancer-non-CVD mortality													
Model 1	0.52	(0.16-1.63)	1	0.90	(0.68-1.18)	1.01	(0.75-1.36)	1.26	(0.90-1.77)	1.20	(0.76-1.90)	0.86	(0.45-1.66)
Model 2	0.52	(0.16-1.64)	1	0.90	(0.69-1.19)	0.98	(0.73-1.32)	1.28	(0.92-1.80)	1.15	(0.72-1.83)	0.80	(0.42-1.55)
Model 3	0.48	(0.15-1.51)	1	0.89	(0.67-1.17)	0.96	(0.71-1.30)	1.22	(0.87-1.71)	1.14	(0.72-1.80)	0.80	(0.41-1.55)
Women													
All-cause mortality													
Model 1	1.45	(0.97-2.18)	1	1.10	(0.94-1.29)	1.19	(1.00-1.42)	1.49	(1.22-1.81)	1.50	(1.14-1.97)	2.05	(1.53-2.74)
Model 2	1.47	(0.98-2.20)	1	1.10	(0.94-1.28)	1.16	(0.97-1.39)	1.45	(1.18-1.77)	1.45	(1.11-1.91)	1.99	(1.48-2.65)
Model 3	1.41	(0.94-2.12)	1	1.10	(0.94-1.29)	1.17	(0.98-1.40)	1.40	(1.14-1.71)	1.41	(1.07-1.85)	1.96	(1.47-2.62)
CVD mortality													
Model 1	0.85	(0.35-2.09)	1	1.07	(0.83-1.38)	1.35	(1.02-1.77)	1.32	(0.96-1.83)	1.67	(1.12-2.50)	1.74	(1.08-2.82)
Model 2	0.85	(0.35-2.11)	1	1.08	(0.84-1.40)	1.33	(1.00-1.75)	1.30	(0.94-1.81)	1.60	(1.07-2.40)	1.74	(1.07-2.82)
Model 3	0.81	(0.33-1.99)	1	1.08	(0.84-1.40)	1.34	(1.01-1.77)	1.21	(0.87-1.69)	1.57	(1.05-2.36)	1.74	(1.07-2.82)
Cancer mortality													
Model 1	1.47	(0.76-2.83)	1	1.15	(0.88-1.52)	0.98	(0.70-1.37)	1.32	(0.91-1.93)	1.39	(0.83-2.35)	2.36	(1.43-3.89)
Model 2	1.43	(0.74-2.77)	1	1.16	(0.88-1.53)	0.98	(0.70-1.38)	1.33	(0.91-1.94)	1.38	(0.82-2.33)	2.37	(1.44-3.92)
Model 3	1.38	(0.71-2.67)	1	1.17	(0.89-1.54)	1.00	(0.71-1.40)	1.29	(0.88-1.89)	1.33	(0.79-2.26)	2.32	(1.40-3.84)
Non-cancer-non-CVD mortality													
Model 1	2.30	(1.22-4.34)	1	1.12	(0.84-1.50)	1.24	(0.90-1.71)	1.90	(1.35-2.69)	1.39	(0.82-2.36)	2.37	(1.40-4.01)
Model 2	2.36	(1.25-4.46)	1	1.11	(0.83-1.48)	1.17	(0.85-1.62)	1.81	(1.28-2.56)	1.36	(0.81-2.31)	2.18	(1.28-3.70)
Model 3	2.32	(1.22-4.39)	1	1.12	(0.84-1.49)	1.20	(0.86-1.65)	1.78	(1.26-2.53)	1.32	(0.78-2.24)	2.19	(1.29-3.72)

Model 1: adjusted for age, town of residence and fasting time (and sex if for all)

Model 2: additionally adjusted for marital status, three main meals per day and physical activity score

Model 3: additionally adjusted for CVD risk factors: smoking, BMI, total cholesterol and blood pressure

Reference: NFG1: 3.8-4.9 mmol/L

Population sample: 7,800 participants of NRP 1A, 3,607 male and 4,193 female, Switzerland 1977-1979, 16-92 years at baseline



**Table S5.** Adjusted hazard ratios for all-cause mortality, by age group and glucose category

	LFG ≤3.8		NFG1 3.8-4.9	NFG2 5.0-5.5		IFG1 5.6-6.0		IFG2 6.1-6.9		DM ≥7.0 mmol/L		KDM	
	HR	(95% CI)		HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
all ages													
Model 1	1.38	(1.04-1.84)	1	1.06	(0.95-1.18)	1.06	(0.94-1.20)	1.31	(1.14-1.50)	1.39	(1.16-1.67)	1.65	(1.35-2.03)
Model 2	1.42	(1.06-1.89)	1	1.06	(0.94-1.18)	1.03	(0.91-1.17)	1.28	(1.11-1.47)	1.33	(1.11-1.60)	1.58	(1.29-1.95)
Model 3	1.35	(1.01-1.80)	1	1.04	(0.93-1.16)	1.01	(0.89-1.14)	1.19	(1.04-1.37)	1.27	(1.05-1.52)	1.55	(1.26-1.90)
16-39 years													
Model 1	1.19	(0.58-2.46)	1	0.84	(0.62-1.12)	1.23	(0.88-1.72)	1.70	(1.15-2.52)	1.55	(0.83-2.91)	0.99	(0.40-2.44)
Model 2	1.24	(0.60-2.56)	1	0.84	(0.63-1.13)	1.22	(0.87-1.70)	1.63	(1.10-2.42)	1.49	(0.80-2.80)	0.90	(0.37-2.23)
Model 3	1.21	(0.59-2.51)	1	0.84	(0.63-1.13)	1.21	(0.86-1.70)	1.58	(1.06-2.35)	1.48	(0.79-2.77)	0.95	(0.38-2.33)
40-64 years													
Model 1	1.44	(0.98-2.10)	1	1.10	(0.94-1.27)	1.06	(0.90-1.25)	1.25	(1.03-1.51)	1.34	(1.04-1.72)	1.76	(1.32-2.36)
Model 2	1.46	(0.99-2.14)	1	1.09	(0.94-1.27)	1.05	(0.89-1.24)	1.25	(1.04-1.52)	1.31	(1.01-1.69)	1.73	(1.29-2.32)
Model 3	1.36	(0.93-1.99)	1	1.04	(0.90-1.21)	1.00	(0.84-1.18)	1.13	(0.93-1.37)	1.19	(0.92-1.54)	1.60	(1.19-2.15)
65-92 years													
Model 1	1.41	(0.80-2.46)	1	1.15	(0.94-1.42)	1.04	(0.84-1.29)	1.39	(1.08-1.78)	1.47	(1.09-1.98)	1.69	(1.23-2.32)
Model 2	1.50	(0.85-2.63)	1	1.16	(0.94-1.42)	1.00	(0.80-1.24)	1.33	(1.04-1.71)	1.38	(1.02-1.87)	1.58	(1.15-2.18)
Model 3	1.41	(0.80-2.47)	1	1.17	(0.95-1.44)	1.01	(0.81-1.26)	1.31	(1.02-1.69)	1.38	(1.02-1.87)	1.62	(1.17-2.23)

Model 1: adjusted for age, sex, town of residence and fasting time

Model 2: additionally adjusted for marital status, three main meals per day and physical activity score

Model 3: additionally adjusted for CVD risk factors: smoking, BMI, total cholesterol and blood pressure

Reference: NFG1: 3.8-4.9 mmol/L

Population sample: 7,800 participants of NRP 1A, 3,607 male and 4,193 female, Switzerland 1977-1979, 16-92 years at baseline

**Table S6.** Adjusted hazard ratios for all-cause mortality, by glucose category, sex and increasing years of follow-up

	LFG <3.8		NFG1 3.8-4.9	NFG2 5.0-5.5	IFG1 5.6-6.0		IFG2 6.1-6.9		DM ≥7.0 mmol/L		KDM		
	HR	(95% CI)		HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)	HR	(95% CI)
All participants													
5 years	1.77	(0.74-4.23)	1	1.18	(0.77-1.80)	1.19	(0.76-1.87)	1.05	(0.63-1.76)	1.64	(0.92-2.93)	1.65	(0.87-3.13)
10 years	1.36	(0.73-2.56)	1	1.11	(0.85-1.44)	1.11	(0.83-1.48)	1.41	(1.04-1.92)	1.62	(1.12-2.34)	1.82	(1.22-2.73)
15 years	1.25	(0.76-2.04)	1	1.14	(0.94-1.39)	1.05	(0.85-1.31)	1.41	(1.12-1.77)	1.45	(1.08-1.95)	1.53	(1.10-2.13)
20 years	1.34	(0.90-1.98)	1	1.08	(0.92-1.27)	1.07	(0.90-1.27)	1.37	(1.14-1.66)	1.45	(1.14-1.85)	1.53	(1.16-2.00)
25 years	1.52	(1.11-2.10)	1	1.11	(0.97-1.26)	1.07	(0.92-1.24)	1.35	(1.15-1.59)	1.40	(1.13-1.73)	1.60	(1.27-2.02)
30 years	1.37	(1.02-1.83)	1	1.02	(0.91-1.15)	1.01	(0.89-1.15)	1.21	(1.04-1.39)	1.25	(1.03-1.50)	1.54	(1.25-1.90)
all years	1.35	(1.01-1.80)	1	1.04	(0.93-1.16)	1.01	(0.89-1.14)	1.19	(1.04-1.37)	1.27	(1.05-1.52)	1.55	(1.26-1.90)
Men													
5 years	1.66	(0.57-4.87)	1	0.98	(0.57-1.69)	1.18	(0.68-2.04)	0.72	(0.35-1.47)	1.51	(0.73-3.10)	1.51	(0.67-3.43)
10 years	1.24	(0.56-2.74)	1	0.94	(0.67-1.33)	0.92	(0.64-1.32)	1.22	(0.83-1.79)	1.49	(0.94-2.35)	1.45	(0.86-2.46)
15 years	1.27	(0.69-2.32)	1	0.95	(0.73-1.23)	0.89	(0.67-1.17)	1.19	(0.88-1.60)	1.25	(0.85-1.82)	1.20	(0.76-1.89)
20 years	1.22	(0.71-2.08)	1	0.97	(0.78-1.21)	0.96	(0.76-1.21)	1.22	(0.94-1.58)	1.27	(0.92-1.75)	1.21	(0.82-1.78)
25 years	1.49	(0.95-2.32)	1	1.02	(0.84-1.23)	0.91	(0.74-1.12)	1.19	(0.95-1.49)	1.23	(0.92-1.63)	1.32	(0.94-1.84)
30 years	1.31	(0.86-1.99)	1	0.95	(0.81-1.12)	0.91	(0.76-1.08)	1.04	(0.85-1.27)	1.10	(0.85-1.43)	1.22	(0.90-1.65)
all years	1.32	(0.87-1.99)	1	0.97	(0.83-1.13)	0.90	(0.76-1.07)	1.04	(0.85-1.27)	1.13	(0.88-1.45)	1.24	(0.92-1.67)
Women													
5 years	2.14	(0.47-9.71)	1	1.40	(0.70-2.80)	1.08	(0.48-2.40)	1.54	(0.69-3.44)	1.39	(0.51-3.83)	2.06	(0.72-5.90)
10 years	1.80	(0.63-5.14)	1	1.35	(0.87-2.09)	1.46	(0.91-2.35)	1.80	(1.08-2.98)	1.71	(0.90-3.26)	2.46	(1.30-4.64)
15 years	1.26	(0.54-2.93)	1	1.42	(1.04-1.93)	1.37	(0.97-1.93)	1.81	(1.26-2.61)	1.72	(1.06-2.77)	2.00	(1.22-3.29)
20 years	1.60	(0.90-2.85)	1	1.21	(0.96-1.53)	1.24	(0.95-1.60)	1.59	(1.20-2.10)	1.65	(1.15-2.37)	1.93	(1.32-2.82)
25 years	1.61	(1.01-2.57)	1	1.19	(0.99-1.44)	1.29	(1.05-1.60)	1.58	(1.25-1.99)	1.56	(1.14-2.13)	1.95	(1.40-2.71)
30 years	1.46	(0.96-2.20)	1	1.09	(0.93-1.28)	1.16	(0.96-1.39)	1.43	(1.17-1.76)	1.39	(1.05-1.84)	1.97	(1.47-2.64)
all years	1.41	(0.94-2.12)	1	1.10	(0.94-1.29)	1.17	(0.98-1.40)	1.40	(1.14-1.71)	1.41	(1.07-1.85)	1.96	(1.47-2.62)

Population sample: 7,800 participants of NRP 1A, 3,607 male and 4,193 female, Switzerland 1977-1979, 16-92 years at baseline

Glucose categories: LFG: <3.8 mmol/L, NFG1: 3.5-4.9 mmol/L, NFG2: 5.0-5.5 mmol/L, IFG1: 5.6-6.0 mmol/L, IFG2: 6.1-6.9 mmol/L,

DM: diabetes ≥7 mmol/L, KDM: known diabetes. Reference: NFG1: 3.8-4.9 mmol/L

Adjusted for age, fasting time, town of residence, marital status, three main meals per day, physical activity, smoking, BMI, cholesterol, blood pressure and additionally sex if for all participants.

**Figure S7.** Adjusted hazard ratios (HR and 95% CI) for all-cause mortality, by low glucose category <3.8 mmol/L and all participants over increasing years of follow-up and additionally over 25 and 32 years after exclusion of deaths within the first 5 years (\*). Adjustments for age, sex, town of residence, marital status, physical activity, three meals per day, blood pressure, smoking, BMI and total cholesterol. Reference: NFG1= 3.8-4.9 mmol/L. Population sample: 7,800 participants of NRP 1A, 3,607 male and 4,193 female, Switzerland 1977-1979, 16-92 years at baseline

